INSTITUTE OF PUBLIC HEALTH

COLLEGE OF MEDICINE AND HEALTH SCIENCES
UNIVERSITY OF GONDAR

PREVALENCE AND ASSOCIATED FACTORS OF LOW BIRTH WEIGHT AND PRETERM DELIVERY AMONG INFANT BORN TO HIV INFECTED WOMEN IN PUBLIC HOSPITALS OF NORTH GONDAR, NORTHWEST ETHIOPIA, 2012

By; Bekana Kebede (BSC public Health)

Advisor; Mr.Gashaw Andargie (MPH, PHD candidate)

A THESIS SUBMITTED TO INSTITUTE OF PUBLIC HEALTH, COLLEGE OF MEDICINE AND HEALTH SCIENCES, UNIVERSITY OF GONDAR IN PARTIAL FULLFILMENT OF THE REQUIRMENT FOR THE DEGREE OF MASTERS OF PUBLIC HEALTH.

JUNE, 2012

Gondar, Ethiopia

INSTITUTE OF PUBLIC HEALTH

COLLEGE OF MEDICINE AND HEALTH SCIENCES

UNIVERSITY OF GONDAR

PREVALENCE AND ASSOCIATED FACTROS OF LOW BIRTH WEIGHT AND PRETERM DELIVERY AMONG INFANT BORN TO HIV INFECTED WOMEN IN PUBLIC HOSPITALS OF NORTH GONDAR, NORTHWEST ETHIOPIA, 2012

By; Bekana Kebede (BSc Public Health)

Email:bekanakeb@yahoo.com

Tell:+251-912017603

Approved by examining board

_____ _____

Head, institute of Public Health

Advisor:

Mr.Gashaw Andargie _____

_____ _____

Examiner

Table of Content

Contents **page**

ACKNOWLEDGEMENT

I am indebted to my advisor, Mr.Gashaw Andargie for his constructive criticism, patience, encouragement and support throughout the course of this research study. He so willingly sacrificed much of his personal time to make this thesis a reality. Staffs of the university of Gondar, college of Medicine and Health Sciences are thanked for their valuable input. I am extremely grateful to Mr. Abebaw Gebeyehu for his generous constructive criticism and extreme patience, advice and his input and involvement during analysis of the data, and Mr.Mekuriaw Alemayehu and Mr.Solomon Meseret for their constructive comment, during analysis of the result. I would also like to extend my heartfelt gratitude to all my colleagues, fellow students and lecturers of my MPH class. Finally I would like to extend my appreciation to Gondar University Hospital staffs, ,Dr.Samuel Astatikachew(Metemma Hospital medical director) and Dr. Andinet Debark Hospital medical director),I tech Ethiopia and other staffs for their support during data collection in data base access and data collection assistants. This research study is financially supported by University of Gondar, college of Medicine and Health Science.

Acronyms

ANC-Antenatal Care

APH-Antepartum Hemorrhage

ARVs-Antiretrovirals

ART-Antiretroviral Treatment

AZT-Zidovudine

BMI-Body Mass Index

DM-Diabetes Mellitus

FMOH-Federal Ministry of Health

HMIS-Health Management Information System

HIV-Human Immune Virus

HAART-Highly Active Antiretroviral Treatment

HTN-Hypertension

IUGR-Intrauterine Growth Retardation

LBW-Low Birth Weight

MTCT-Mother to Child Transmission

PD-Preterm Delivery

PMTCT-Prevention of Mother to Child Transmission

PI- Protease Inhibitors

PROM-Premature Rupture of Membrane

SGA-Small for Gestational Age

sdNVP-Single Dose Nevirapine

STI-Sexually Transmitted Infection

TB-Tuberculosis

UTI-Urinary tract Infection

WHO-World Health Organization

LIST OF TABLES AND FIGURES

List of tables

List of Figures

ABSTRACT

Background: HIV in pregnancy is one of the commonly documented challenge and pregnancy complication and HIV positive pregnant women are at a significantly increased risk of adverse pregnancy outcomes such as lower birth weight, preterm birth and perinatal death. Identifying factors associated with the adverse birth outcome would lead to better improvement in intervention.

Objective: the objective of this study was to assess the prevalence and associated factors of low birth weight and preterm birth among infant born to HIV infected women in Public Hospitals in North Gondar, Northwest Ethiopia.

Methods*:* Institutional based cross-sectional study was conducted. All infant born to HIV infected women during September 1, 2009 to April 30, 2012 was included in the study by extracting recorded data of the mothers and infant birth in public hospitals of North Gondar Zone, Northwest Ethiopia. Then both bivariate and multivariate-logistic regression was performed using 95% confidence interval and respective odds ratio was determined.

Result: Out of 416 singletons infant born to HIV infected mothers the prevalence of low birth weight and preterm delivery was 89(21.4 %) and 69(16.6 %) respectively. Baseline maternal CD4 count level below 200cells/mm3 [AOR (95%C.I.)= 4.24(1.85, 9.69)], maternal BMI below 18.5 [AOR (95%C.I.)= 5.50(2.82, 10.74)], gestational age at birth below 37weeks, [AOR (95%C.I) =28.14(12.69, 62.34)] and maternal exposure to HAART [AOR (95%C.I) =8.26(2.53, 14.24)] were factors significantly associated with LBW. On the other hand, baseline maternal CD4 level below 200/mm3[AOR(95%CI)= 5.37(1.89, 15.49)],having no PMTCT intervention during pregnancy [AOR (95%C.I) =1.53(1.24, 3.05)], maternal BMI less than 18.5[AOR(95%C.I)=4.50(2.39, 9.27)], mother who had already started HAART before pregnancy [AOR(95%C.I)=1.82(1.02,3.81)] were factors associated with preterm delivery.

Conclusion and recommendation: This study showed that the prevalence of low birth weight and preterm delivery among infant born to HIV positive mothers is very high. Maternal low baseline CD4 level, low BMI, exposure to HAART, and preterm delivery were associated factors of LBW, and similarly, low baseline maternal CD4 level, low BMI,having no PMTCT intervention and maternal being on HAART before pregnancy were factors associated with PD.

The programme for PMTCT services should give attention in early identification of those mothers with predicted complication like those with low CD4 level or advanced clinical stage, to link them to appropriate intervention like family planning, and timely treatment intervention and infection-prevention.

1. INTRODUCTION

1.1 Statement of the problem

Human immunodeficiency virus continues to take a heavy toll on women and children worldwide(1). In 2008, 33.4 million individuals were living with HIV, of whom 15.7 million were women and 2.1 million were children under 15 years of age (1, 2) and about 3 million people are currently estimated to be receiving antiretroviral therapy(ART) in low- and middle income countries of which 56% of people receiving ART were women.(1)

HIV infection in pregnancy has become the most common complication of pregnancy in some developing countries. WHO thus now recommends the initiation of HAART in pregnancy for all HIV-infected women with CD4 cell counts <350 cells/mm3 irrespective of WHO clinical staging, and for all women in WHO clinical stage 3 or 4, irrespective of the CD4 cell count and as a PMTCT option for all HIV-infected women (3) to maximize prevention of HIV transmission and maternal and infant survival(3, 4) .

Based on this in 2009, 53% of the estimated HIV-infected pregnant women worldwide received at least some antiretroviral (ARV) drugs to prevent HIV transmission to their child (5).

In Ethiopia In 2009, there were an estimated 84,189 HIV-positive pregnancies and 14,093 HIV-positive births and based on the single point estimate of HIV/AIDS prevalence of HAPCO and has estimated HIV prevalence of 2.4% with more than 1 million people living with HIV in 2010 (6, 7)

Early HAART initiation for all HIV-positive pregnant women (2, 8) and widespread use of HAART among HIV infected pregnant women has led to dramatic decreases in HIV transmission to the infant (9, 10) and decreases maternal morbidity(11-13). Currently, MTCT prevention programs in sub-Saharan African countries include zidovudine and Lamivudine during the final weeks of pregnancy and sd-NVP at delivery.(2, 4, 14)

However, HIV infection, use of such medications during pregnancy for which adverse pregnancy and fetal outcomes are not completely known and many uncertainities remain regarding potential adverse effects of HAART initiation and use in pregnancy on the birth outcome. Low birth weight and preterm delivery are the commonly reported adverse outcomes among HIV infected women (13).

An adverse Birth outcome like low birth weight and preterm birth is associated with maternal HIV infection, maternal CD4 level, duration on HAART, time of HAART initiation and type of HAART regimen. The risk of having a low-birth-weight baby was substantially and significantly increased with maternal HIV infection. But still there remain controversies in between different studies in different countries (15-17).

Based on epidemiological observations that infants weighing less than 2,500 g are approximately 20 times more likely to die than heavier babies (18).More than 20 million infants worldwide, representing 15.5 per cent of all births are born with low birth weight, 95.6 per cent of them in developing countries. Low birth weight levels in sub-Saharan Africa are around 15 per cent.

Existing research on the determinants of LBW also focuses primarily on nutritional determinants in industrialized countries. LBW is caused by retarded growth in utero, shortened gestation, or both. Low prepregnancy weight and poor pregnancy weight gain have been identified as the strongest determinants of intrauterine growth retardation leading to LBW(19) .

This study was aimed at identifying the prevalence and associated factors of low birth weight and preterm delivery among infant born to HIV infected mothers. The study was conducted in the Public Hospitals in North Gondar, Northwest Ethiopia.

1.2 Literature Review

Birth outcome can be affected by maternal prepregnancy related infections and nutritional status and on pregnancy weight gain other related factors including on pregnancy drug intake, infections and complications. Low birth weight is defined as newborn birth weight below 2.5kg at birth and preterm birth is defined as birth of infant at below 37 complete weeks of gestation according to WHO(20). Current studies are revealing the high occurrence of low birth weight and preterm birth among HIV infected pregnant women.

Preterm birth and low birth weight are the most common direct cause of newborn mortality. Preterm birth and SGA, which are the reasons for low-birth-weight (LBW), are also important indirect causes of neonatal deaths. LBW contributes to 60% to 80% of all neonatal deaths. The global prevalence of LBW is 15.5%, which amounts to about 20 million LBW infants born each year, 96.5% of them in developing countries. Countries can reduce their neonatal and infant mortality rates by improving the care of LBW infants mortality(21).

1.2.1 Maternal HIV infection and Birth Outcome

Human immunovirus (HIV) is the leading cause of morbidity and mortality among women of reproductive age. It has been estimated that, 1.4 million HIV-infected women gave birth in low- and middle-income countries in 2008 where 91% of whom reside in sub-Saharan Africa.(2)

In Ethiopia the prevalence of HIV among those pregnant mothers who underwent HIV testing is 8% where the number of HIV positive pregnant mothers identified per year has increased from 4,172 in 2006 to 13,257 in 2010 and 53% of known HIV-positive mothers and 48% of known HIV-exposed infants have received ARV prophylaxis according to recent five-year national level PMTCT data analysis(7).

While HIV/AIDS is not a major direct cause of neonatal death, maternal HIV status affects newborn survival by causing an increased risk of preterm,lowbirth weight and death in the neonatal period and infancy, even among those babies who do not become HIV-positive.(22) Newborns of HIV-positive women are more likely to be very low birth

weight (LBW), preterm and have low Apgar scores, placing them at greater risk of death. The interaction of HIV with other infections and the indirect effects of HIV, such as poverty and maternal illness, also contribute to poor outcomes for newborns. (23)

Early studies on the association between maternal HIV infection and adverse perinatal outcome showed as there appears to be an association, between maternal HIV infection and an adverse perinatal outcome(24). A cohort studies have reported that prematurity was almost twice more frequent in infant born to HIV positive women than infant born to HIV negative women. The proportion of LBW infants was twice as high as among newborn of HIV positive women than HIV negative women. Similarly, the frequency of IUGR was almost three times higher in infant born to HIV positive women than HIV negative women(25, 26).HIV infection is associated with PTD, with a 2.5-fold increased risk. HIV infection conferred a 2.1-fold increased risk for spontaneous PTD, and a 3.2-fold increased risk for iatrogenic PTD.(27) .Recent longitudinal study conducted in china indicated the prevalence of LBW and Preterm delivery among 194 HIV-positive mothers which was 19.6% and 9.8% , respectively(28).

A longitudinal study conducted in 2007 in South Africa found that an adverse pregnancy outcome was independently associated with HIV-infected women and Birth weight was inversely associated with maternal HIV(16).

Studies from Kenya showed HIV-infected women were 3 times more likely to deliver a low birth- weight baby, especially in the presence of HIV-related symptoms (25, 29) and in Rwanda also , low birth weight was significant in babies of asymptomatic women than in babies born to uninfected women(23).Findings of study in Mozambique showed as there was a trend towards increased rates among HIV-positive women for most of these outcomes and infants born to HIV-positive women had more than twice a higher risk of death than infants born to HIV-negative women(14).

As to the study in India, compared with infants of HIV-infected women enrolled during antenatal, infants of HIV-infected women enrolled in the post-partum ward had a higher risk of pre-term delivery (20% versus 8%) and LBW (41% versus 22%) and the prevalence of low birth weight infants among HIV-infected pregnant women was 12.6%(30).

1.2.2 Maternal ARV exposure and birth outcome

During pregnancy, healthcare providers in high income countries recommend initiation of HAART for all HIV-infected women in order to reduce viral load, improve maternal health, and prevent perinatal HIV transmission(31). In some resource-poor settings, initiating HAART has been recommended only for pregnant women with more advanced HIV disease [i.e., CD4 cell count<200 cells/ml (<250 cells/ml) or HIV-related symptoms and CD4 cell count<350 cells/ml] (32).

Antenatal provision of cotrimoxazole for HIV-infected pregnant women with low CD4 cell counts may have indirect benefits for neonatal health(33). Antenatal provision of cotrimoxazole for HIV-infected pregnant women with low CD4 cell counts have reduced trends in low birth weight, preterm delivery and neonatal mortality as compared to those HIV infected mother not on antenatal cotrimoxazole prophylaxis and similarly co-trimoxazole reduces chorioamnionitis with associated reduction in severe pre-term delivery rates and improved infant mortality as to study conducted in USA(34) and zambia (35).

Mother to child transmission rates were lower in women who became pregnant on HAART than those initiating HAART during pregnancy and Late initiation of HAART is associated with increased risk of MTCT(36).However, HAART exposure was associated with an increased preterm birth rate and more advanced immune-suppression was a risk factor for low birth weight and preterm birth (15, 37-39). Indeed, in HIV-infected women taking HAART, iatrogenic PTD contributes up to 40% of the overall prematurity. The use of HAART during the second half of pregnancy was strongly associated with iatrogenic PTD compared with women untreated during pregnancy (27).

Various types of ARVs drug and no ARV were associated with LBW. Low birth weight infants delivered from HIV-infected pregnant women with and without ART were 9.9% (7/41) and 13.6% (19/159), respectively. The one who received HAART had 2.27 times higher risk in having LBW (40) and women who were using ARVs pre-conception had higher rates of LBW and PTD (33.3% vs 16.5% and (26.3% vs. 17.7%) respectively (38, 41). In line with this study conducted by European collaborative study observed a 2.1-fold increased risk when HAART was started before pre-conception and 1.9-fold

increased risk of delivery at less than 37 weeks of gestation when HAART was started late during pregnancy (42, 43)and the risk of delivery before 34 weeks' gestation was increased by 2.5-fold for those starting combination ARV regimens during pregnancy and 4.4-fold for those entering pregnancy on combination ARV regimens(42).

This study is also supported by study conducted in Poland (39) which revealed that Pre-term deliveries were highly prevalent among women on HAART during pregnancy, especially when therapy was started before or in the first trimester of pregnancy and women receiving HAART with PI were at a higher risk of delivering a baby with low birth weight.

Compared with 2-drug therapy, women who did not take ARV drugs, as well as those who took only 1-drug or 3-drug combinations had increased risks of preterm birth as indicated on study in USA (44) and low birth weight was associated with a history of illicit maternal drug use, unknown maternal HIV status before delivery, symptomatic maternal HIV disease, and infant HIV infection and preterm birth was associated with a history of illicit maternal drug use, symptomatic maternal HIV disease, no ART, receipt of a 3-drug HAART regimen with PIs, and infant HIV infection. But exposure to monotherapy was not associated with prematurity as European collaborative study (41)

In contrast, the use of multiple ARV drugs compared with no drugs or treatment with one drug was not associated with increased rates of preterm labor, low birth weight, low Apgar scores, or stillbirth (45) nor were any significant associations between adverse pregnancy outcome and use of ARV drugs by class/regimen or by category (including combination ARV regimens) found in an analysis from the Women and Infants Transmission Study (WITS) and study in England(46, 47). Additionally prospective cohort study of 681 women from South American and Caribbean countries who received at least 1 antiretroviral drug did not find a significant association between premature delivery and ART during pregnancy (48) and meta-analysis of 14 European and American clinical studies found no increase in risk of PD with either any ARV drug receipt compared with no drugs or combination of ARV regimens including PIs compared with no drugs (12) and the risk of LBW and stillbirth were not increased in any drug regimen groups(49).

Several studies from sub-Saharan Africa also suggested that HIV-infected mothers may be at increased risk of adverse pregnancy outcomes (50) and enhanced prenatal care is important to improved birth outcomes among HIV-Infected women (51) and recent cohort study in Nigeria has shown that compared to HIV infected mother who where on HAART during early pregnancy Intrauterine growth restriction (IUGR), PD, frequency of LBW were significantly higher among women with untreated-HIV infection in pregnancy(52).

A study in Abidjan, Côte d'Ivoire, compared women eligible for HAART from two cohorts, each with approximately 150 women(53) . LBW was two-fold higher in the cohort that took three-drug HAART compared with the cohort that received two-drug, short-course ARV prophylaxis for preventing MTCT. LBW rates were highest in those who had initiated HAART prior to pregnancy. A larger study in Botswana found that HAART-exposed infants were smaller for gestational age than unexposed infants (54).

Specific HAART regimens, early exposure to any regimen was associated with PD compared with HAART-unexposed infants. Women receiving HAART with PI were at a higher risk of delivering a baby with low birth weight.(39) It should be noted that women who received PI-containing HAART had more advanced HIV disease or had experienced failure of other antiretroviral regimens; advanced maternal HIV disease is a recognized risk factor for preterm delivery (9, 55, 56) Among women with early HAART-exposure, higher rates of LBW were observed in women receiving Efavirenz based regimens compared with nevirapine and PIs-based regimens. Even though there were no differences in rates of LBW by regimen in the late HAART initiated group(15).

A prospective study in Germany and Austria also indicated that use of antenatal PI-based HAART initiated before or during pregnancy was associated with a significantly increased risk of premature delivery [AOR =3.40], compared with monotherapy. the mean birth weight z-score for children exposed to HAART with PI or dual therapy was slightly but significantly higher than that for those exposed to monotherapy(57).However other study showed that combination of ARV with PI was not significantly associated with spontaneous preterm birth, compared to ARV without PI and Low birth weight result is similar. (58)

1.2.3 Maternal immunity level and birth outcome

As CD4 level is also the main correlates of adverse pregnancy outcome as the study reveals, women with a CD4 count <200 cells/mL were nearly twice as likely to have an adverse pregnancy outcome than those with a cell count of 500 cells/mL or more (16) and With each 50 cells/mm3 increase in CD4 cell count associated with a 57% reduction in the odds of LBW (15-17, 59).

These studies are also supported by study in china indicating Lower CD4 cell count; <100 cell/μl and CD4 cell count 100–199 cells/μl compared to CD4 ≥350 cells/μl and higher HIV RNA viral load [≥100 000 copies/ml at enrollment, gestational age at delivery (<37 weeks) were associated with higher risk for LBW. But for PD, only maternal injection drug use as the route of HIV transmission compared to those infected with HIV through sexual transmission was significantly associated with a higher risk of preterm delivery. Mothers infected through drug use were 5.30-fold more than those infected via sexual transmission.(28)

However, one recent multi-centric study depicted as there is no difference in LBW and PD among cohort of mothers with <200 CD4 cells and >500 CD4 cells respectively(60)

Finally study dealing with the birth outcome particularly of low birth weight and preterm birth among HIV infected women is limited in Ethiopia and the current study thus will be an opportunity for information and better improvement of newborn health care.

1.3 Justification of the study

Though the government of Ethiopia is working towards achievement of the reduction of prevention of HIV transmission from mother to child as to the recommendation of WHO and country level guideline, some evaluative study for the outcome of the treatment and PMTCT is also very valuable for programe evaluation and intervention. Different studies in different countries remarked and find out different infant birth outcome and factors associated with; among HIV infected women and most of the studies are in controversies.

Particularly in Ethiopia there was no study assessing the infant birth outcome particularly on low birth weight and preterm birth among HIV infected mothers as far as the best of my knowledge is concerned.

Thus the present study was aimed to identify the associated factors of low birth weight and preterm birth among infant born to HIV infected women in Public Hospitals and the study will be the helpful in improvement in medical care for infants, for programmers, community workers and policy makers and also to improve the health outcome of infants in child health programme.

2. OBJECTIVES

2.1 General Objectives

To assess the prevalence and associated factors of Low birth weight and preterm birth among infant born to HIV infected mothers in Public Hospitals in North Gondar, Northwest Ethiopia

2.2 Specific Objectives

- To determine the prevalence of low birth weight among infant born to HIV infected women in Public Hospitals
- To determine the prevalence of preterm birth among infant born to HIV infected women in Public Hospitals
- To identify factors associated with low birth weight among infant born to HIV infected women in Public Hospitals
- To identify factors associated with preterm birth among infant born to HIV infected women in Public Hospitals

3. METHODS

3.1 Study design and period

Institutional based cross-sectional study design was conducted using data extraction format to get data of infant-mother pairs retrospectively from hospital records among infant born to HIV positive women in Public Hospitals during September 1, 2009 to April 10, 2012.

3.2 Study area and setting

The study was conducted in the three Public Hospitals of North Gondar, Northwest Ethiopia (namely Gondar University Hospital, Metema Hospital and Debark Hospital) from March to April 10, 2012. North Gondar Zone is located about 725 km North west of Addis Ababa having a population of about 3,461,225 (61)**.**In the Zone there are 3 government Hospitals, 29 health centers and 449 health posts. According to ANC sentinel surveillance done in 2007, the prevalence of HIV Among antenatal attendants is 3.9%.PMTCT service in the Zone initiated in 2005 and currently there are more than 23 PMTCT clinics in the Zone (62)**.**

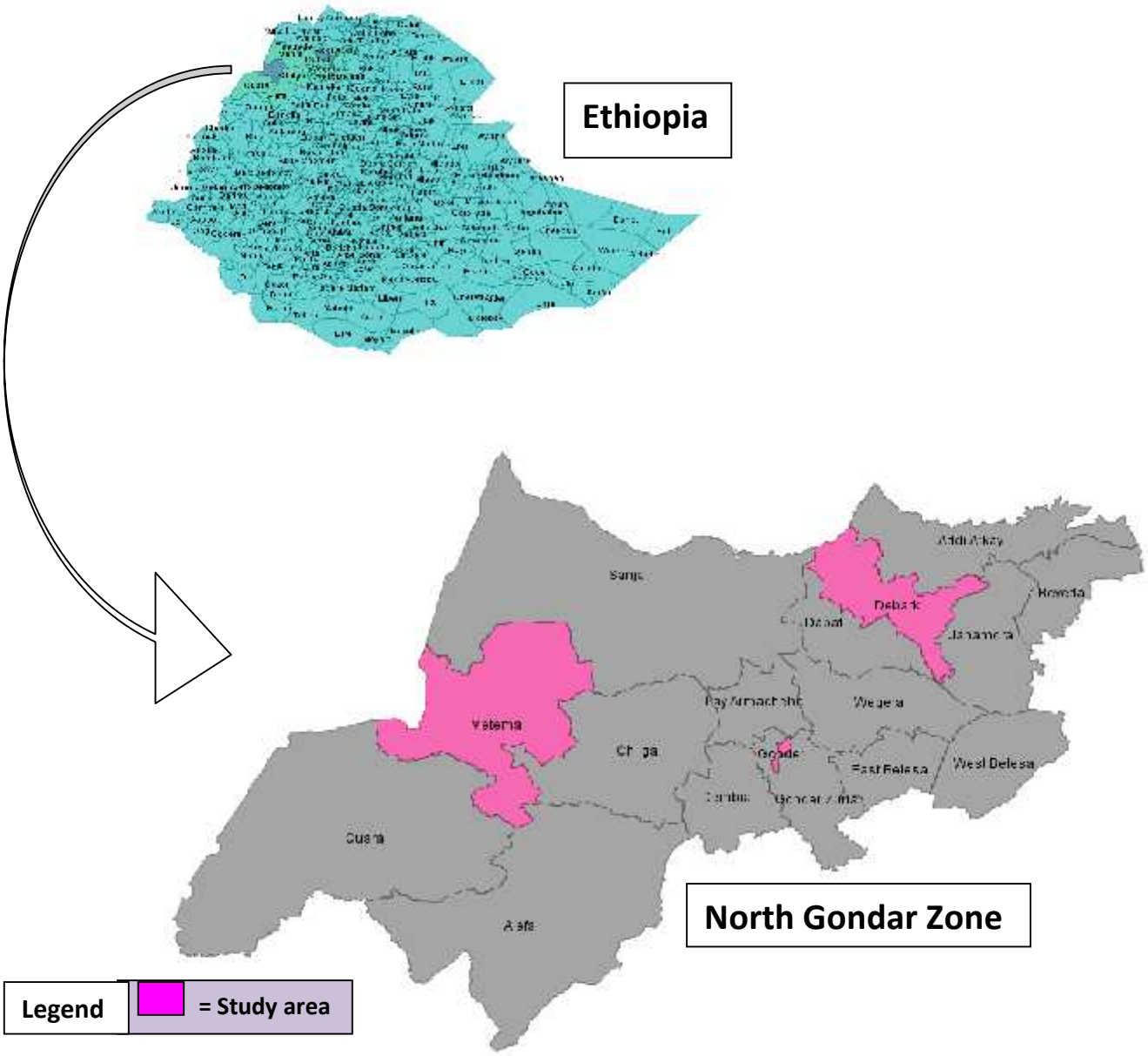

Figure1.The study area (Gondar, Metemma and Debark Hospitals) in North Gondar, Ethiopia

3.3 Source and study population

All Infant born from HIV infected women during September 1, 2009, to April 30, 2012, was the source and as well as the study population.

3.4 Sample size and sampling procedure

Taking 50 % prevalence study since no study in area, 5% margin of error, and 95% confidence interval the sample size was calculated using single population proportion formula to determine minimum sample size as follows:

$$n = \frac{Z^2 . p . (1 - p)}{d^2}$$

$$n1 = \frac{(1.96)2(0.05)(1-0.05)}{(0.05)2}$$

n=384

Thus the final minimum sample size to be involved will be 384. As to sampling procedure all infant born to HIV infected mothers from September 1, 2009 to April 10, 2012 was included in the study population.

3.5 Variables of Study

Dependent variable:

Birth weight and Gestational age at birth

Independent variables:

- Socio-demographic factors of mother :

  Age, parity/gravidity, educational level, religion, occupation, marital status
- Current Obstetric factors:

  Obstetric complications, Mode of labor and delivery
- Maternal nutritional status (maternal anemia,BMI,Wt gain during pregnancy)
- Maternal immunity status:

  CD4 level, WHO clinical stage
- ARVs and related treatment factors:

  Type of PMTC (prophylaxis/HAART) ,Time of HAART initiation,
  Median duration on HAART, ARVs regimen/type
  Cotrimoxazole prophylaxis, Treatment for other co-infections
  Treatment for malaria
- Co-infections or OIs during pregnancy

3.6 Inclusion and Exclusion criteria

Inclusion criteria:

All infant birth from HIV infected women at Public Hospitals during September 2009, to April 2012

Exclusion criteria:

Twin birth

Incomplete or not available infant record

3.7 Operational definitions

Low birth weight (LBW): is defined as a birth weight below 2.5 kg and very low birth weight (VLBW) as less than 1.5 kg.

Preterm delivery (PD): is defined as birth before 37 completed weeks of pregnancy and extremely preterm birth was defined at birth before 34 weeks of pregnancy.

Untreated HIV positive pregnant women: are HIV infected pregnant mothers who had not received antiretroviral drugs during the antenatal period but received nevirapine in labour, also referred to as untreated-maternal HIV infection

3.8 Data collection procedure and quality assurance

The data from HMIS record of the delivery chart and PMTCT / ART follow up chart was extracted which was obtained using pretested and checked data extraction form. The mother PMTCT data was recorded on all information or characteristics including Sociodemographic, maternal weight and enrollment BMI, current and previous obstetric history, drug use and antiretroviral treatment history during ANC follow up, at the ART follow up and during the delivery. The data in the health institution was completed by medical doctors and/or nurses during the follow up of mothers. The information extraction from records was done by using the chart number and identification of mother from PMTCT/ART and delivery charts. BMI was determined by using the mother's prepregnancy weight and Height from their ART/pre-ART follow up.

Gestational age used is those determined by a clinician at the antenatal visit, using a combination of ultrasound (when available), last menstrual period and symphyseal

fundal height examination. The data was extracted by both trained data collection assistant and investigator and the data quality or completeness was checked each time the data obtained.

3.9 Data processing and statistical analysis

Data was entered into Epi info version 3.5.3 and transported to SPSS statistical soft ware version 20 and data was coded, entered, cleaned and analyzed using SPSS. Relevant variables were explained by frequency tables, graphs and Summary statistics.

Maternal information analyzed included demographic characteristics, obstetric history, HIV diseases status, antiretroviral drug (ARV) history including CD4 cell count and WHO stage of disease. The birth outcome evaluated were LBW (<2500 g) and PD (gestational age <37 weeks). Maternal demographic, clinical and obstetrical characteristics were examined within two groups divided by birth weight (<2500 g and ≥2500 g) or gestational age (<37 weeks and ≥37 weeks) for statistical significance by Logistic regression analysis. For two variables (Maternal BMI and pregnancy weight gain) which were having high missing values sensitivity test was done after performing multiple imputation. Multivariate Logistic regression analysis was used to explore the potential risk factors for LBW and PD. All variables in the Univariate analysis with *P* value less than 0.2 were entered into multivariate models using backward stepwise logistic regression. Variables were held in the models if they reached a significance level of P value <0.05. Odds ratio and 95% confidence intervals were also constructed along with its corresponding p-value.

3.10 Ethical clearance

Ethical clearance was obtained from Ethical Review Board of Institute of Public Health College of Medicine and Health Sciences, University of Gondar. Confidentiality of data was kept by avoiding or restricting the use of data by others. Permission was obtained from medical director of the hospital or institutions of data collections.

Confidentiality was ensured from all the data collectors and principal investigator side via using code numbers and keeping questionnaires restricted. No individual patient consent was deemed necessary as this was an anonymous chart/database review. Personal information remained confidential and personal practices were not identified.

5. RESULT

5.1 Sociodemographic factors

A total of 416 babies of HIV infected women who born in the hospitals were included in the study. The mean age of the mothers was 27.27[±4.5] and 361(86.8 %) are Orthodox in religion. Majority, 360(86.5 %) were from urban and about half of the mother were housewife. While about 181(45.7 %) were uneducated, 103(25.7 %) and 84(20.7 %) attended primary and secondary school respectively. About 262(63 %) are in marriage, while 76(18.3%) of mothers have divorced. Table 1 shows the Sociodemographic characteristics of the mothers

Table 1: Sociodemographic characteristics of the HIV positive mothers who gave birth in Public Hospitals of North Gondar, Northwest Ethiopia from September 2009 to April 30, 2012

characteristics	Frequency	percent
Age of mother (years)		
<19	7	1.7
20-25	146	35.1
26-30	189	45.4
>31	74	17.8
Total	416	100.0
Residence		
Urban	360	86.5
rural	53	12.7
total	413	99.30
Religion		
Orthodox	361	86.8
Muslim	43	10.3
Others	5	1.2
Total	409	98.30
Educational status		
Uneducated	181	43.5
Primary school	103	24.8
Secondary school	84	20.2
College	28	6.7
Higher degree	3	0.7
Total	399	95.90
Occupation of the mother		
Housewife	220	52.90
Daily laborer	76	18.30
Merchant	37	8.9
Local drinking seller	11	2.6

Gov't employee	31	7.5
No occupation	34	8.2
Total	409	98.3
Marital status		
Single	38	9.1
Married	262	63
Divorced	76	18.3
Widowed	24	5.8
Separated	14	3.4
Total	414	99.5
Pregnancy history		
Primigravida	123	29.6
Multigravida	280	67.3
Total	403	96.9

5.2 Maternal HIV disease status and ARV treatment related factors

About 200(48.07 %) mothers were on HAART, and 130(31.25 %) were on pre-ART and given PMTCT prophylaxis during pregnancy and the rest were initiated none and no PMTCT intervention. Out of those mothers who were on HAART where 72(36 %) were already started before their pregnancy and 128(64%) have started on pregnancy respectively**.**

The mean CD4 count level of the mothers during pregnancy was 354.6[±156.8], and the baseline pregnancy WHO clinical stage of the women were stage I, 106(25.5%), stage II 139(33.4%), stage III ,97(23.3%) and stage IV 71(17.1%). About 22(5.3 %), 44(10.6 %), 19(4.6 %) and 26(6.3%) of mothers had record of opportunistic infection related diagnosis of TB, UTI and bacteruria, STI and chronic diarrhea during pregnancy respectively.

5.3 current obstetric history related factors

About 346(83.2%), 45(10.8%), and 25(6%) delivery was spontaneous, assisted/instrumental and operative delivery respectively. Only 8.6% of labor was induced. About 20(4.8 %), 22(5.3%), 14(3.4 %) and 39(9.4 %) of mothers had history of APH, Anemia, eclamsia and PROM during the pregnancy. The mean pregnancy weight gain was 7.6 with ±3.4SD and the mean BMI of mothers was 20.5 with+2.58SD.About 8(1.9%) and 4(1%) of mothers had history of HTN and DM during pregnancy.

Out of 416 infant born to HIV infected mother 224(53.8%) were female and where 377(90.6%) were alive and there were 9(2.2%), 4(1.0%) and 24(5.8%) still birth, congenital malformation and early neonatal death respectively.

Table 2: HIV disease status, ARV use and obstetric factors of the HIV positive mothers who gave birth in Public Hospitals of North Gondar, Northwest Ethiopia from September 2009 to April 30, 2012

Factors	frequency	percent
WHO clinical stage		
Stage I	106	25.5
Stage II	139	33.4
Stage III	97	23.3
Stage IV	71	17.1
total	413	99.3
CD4count level(cells/mm3)		
<200	84	20.2
201-350	122	29.3
>350	181	43.5
total	387	93.02
ARV exposure		
none	86	20.7
HAART	200	48.1
Prophylaxis	130	31.3
total	416	100.0
Time HAART started		
Before pregnancy	72	17.3
On pregnancy	128	30.8
total	200	48.1
PMTCT intervention		
no	86	20.7
yes	330	79.3
total	416	100.0
Infection		
UTI and bacteruria	44	10.6
Tuberculosis	22	5.3
STI	19	4.6
Chronic diarrhea	26	6.3
none	279	67.06
total	390	93.75
Mode of labor		
induced	36	8.7
spontaneous	380	91.3
total	416	100.0

Mode of delivery		
Spontaneous vaginal	346	83.2
Induced/assisted	45	10.8
Operative	25	6.0
total	416	100.0
Maternal BMI		
<18.5	77	18.5
>=18.5	270	64.9
total	347	83.4
Obstetric complications		
APH	20	4.8
Anemia	22	5.3
Eclamsia	14	3.4
PROM	39	9.4
none	311	74.8
total	406	97.7
Infant Birth outcome		
alive	374	89.9
Still birth	13	3.1
Early neonatal death	25	6.0
Congenital malformation	4	1.0
total	416	100.0
Sex of the infant		
male	192	46.2
female	224	53.8
total	416	100.0

5.4 Prevalence of Low birth weight and preterm delivery

Out of 416 singleton infant born to HIV infected mothers the prevalence of low birth weight was 89(21.4 %) with the mean birth weight of 2734.38[±457.33] and the prevalence of preterm delivery was 69(16.6 %). About 55(79.7 %) of preterm were low birth weight. Compared with infants of HIV infected mother who were not exposed to HAART during pregnancy, infants of HIV infected mother who were exposed to HAART had higher prevalence of LBW (5.6% Vs 38.5%) and similarly, compared with Infants of HIV-infected women who were enrolled in PMTCT (either HAART or Prophylaxis), infants of HIV-infected women who were not enrolled in PMTCT had higher prevalence of pre-term delivery (11.6% Vs 23.9%).

The prevalence of LBW and preterm delivery is higher in those mothers with CD4 level below 200cells/mm3 as compared to those having above 350cells/mm3 (46.4% Vs 11.0%) and (45.2% Vs 6.6%) respectively.

The prevalence of LBW among those mothers who were in WHO clinical stage III,33(34.0%) and stage IV, 25(35.2%) were higher than among those in stage I,14(13.2%) and stage II,17(12.2%)and similarly the prevalence of Preterm delivery was 23(32.4%),29(29.9%),10(7.2%) and 7(6.6%) in those in clinical stage IV,III,II and stage I respectively.

Related to obstetric complication the prevalence of low birth and preterm delivery was 14(63.6%), 4(28.6%), 12(30.8%) and the prevalence of preterm delivery was 8(46.4%), 5(35.7%) and 13(33.3%) among those mother having anemia, Eclamsia and PROM respectively.

The following table 3, shows the prevalence of LBW and PD with some selected factors

Table 3: prevalence of LBW and PD among infant born to HIV positive mothers in Public Hospitals of North Gondar, Northwest Ethiopia, from September 2009 to April 2012

Factors	Low birth Weight		Preterm Delivery	
	Frequency	percent	frequency	percent
Age of mother				
<19	1	14.3	1	14.3
20-25	35	24.0	28	19.2
26-30	36	19.0	28	19.2
>31	17	17.0	12	16.2
Residence				
Urban	76	21.1	58	16.1
Rural	12	22.6	10	18.9
Educational status				
Uneducated	40	22.1	33	18.2
Primary school	27	26.2	21	20.4
Secondary school	11	13.1	9	10.7
Tertiary/College	8	28.6	3	10.7
Higher degree	0	0.0	0	0.0
Maternal occupation				
Housewife	46	20.9	40	18.2
Daily laborer	24	31.6	19	25.0
Merchant	5	13.5	3	8.1
Local drinking seller	1	9.1	0	0.0
Gov't employee	7	22.6	3	9.7
No occupation	5	14.7	3	8.8
Marital status				
Single	11	28.9	6	15.8
Married	47	17.9	41	15.6
Divorced	19	25.0	14	18.4
Widowed	6	25.0	5	20.8
Separated	6	42.9	3	21.4
Pregnancy history				
Primigravida	29	23.6	23	18.7
Multigravida	59	21.1	44	15.7
Obstetric complications				
None	56	18.0	40	12.9
APH	2	10.0	2	10.0
Anemia	14	63.6	8	36.4
Eclamsia	4	28.6	5	35.7
PROM	12	30.8	13	33.3
BMI				
<18.499	43	55.8	34	44.2
>18.5	40	14.8	27	10.0

Infections/OIs				
STI	9	47.4	10	45.5
TB	9	40.9	11	50.0
UTI & bacteruria	10	22.7	10	24.4
Chronic diarrhea	7	26.9	4	15.4
PMTCT intervention				
No	45	13.6	79	23.9
Yes	24	27.9	10	11.6
HAART exposure				
No	12	5.6	25	11.6
Yes	77	38.5	44	22.0
Time HAART initiated				
Before pregnancy	44	61.1	22	30.6
On pregnancy	33	25.8	22	17.2
ARV intervention				
None	10	11.6	24	27.9
HAART	77	38.5	44	22.0
Prophylaxis	2	1.5	1	0.80
CD4 level (cell/mm3)				
<200	39	46.4	38	45.2
201-350	30	24.6	19	15.6
>351	20	11.0	12	6.6
WHO clinical stage				
I	14	13.2	7	6.6
II	17	12.2	10	7.2
III	33	34.0	29	29.9
IV	25	35.2	23	32.4
Gestational age at birth				
>=37 weeks	34	9.8		
<37weeks	55	79.7		
Mode of labor				
Induced	5	13.9	6	16.7
Spontaneous	84	22.1	63	16.6
Mode of delivery				
Spontaneous vaginal	77	22.3	56	16.2
Assisted/instrumental	8	17.8	8	17.8
Operative	4	16.0	5	20.0

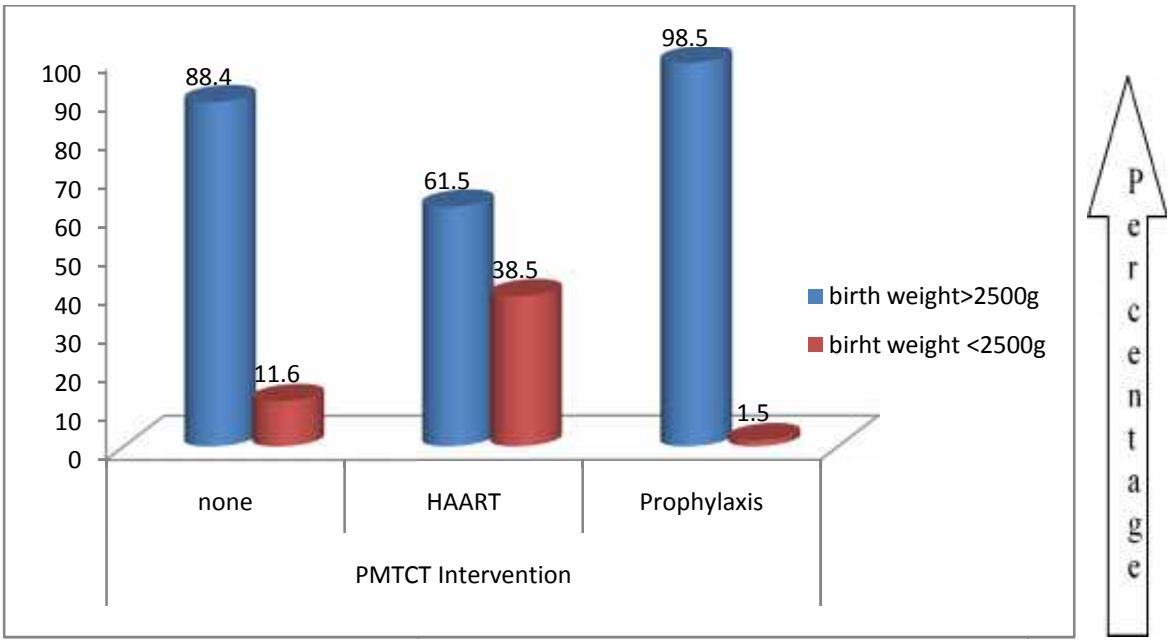

Figure 2. The prevalence of low birth weight with the types of PMTCT intervention given for HIV positive women who gave birth in Public Hospitals in North Gondar Zone, Northwest Ethiopia during September1, 2009 to April 30, 2012

5.5 Factors associated with low birth weight and preterm delivery

The multivariate analysis of factors associated with LBW showed that baseline maternal CD4 count level below 200cells/mm3 [AOR (95%C.I.)= 4.24(1.85, 9.69)], maternal BMI below 18.5 [AOR (95%C.I.)= 5.50(2.82, 10.74)], gestational age at birth below 37weeks, [AOR (95%C.I)=28.14(12.69, 62.34)] and maternal exposure to HAART [AOR (95%C.I) =8.26(2.53, 14.24)] were significantly associated with LBW. Those mother who were having CD4 count level below 200cells/mm3 had 4.2 times higher risk of having low birth weight as compared to those mothers with CD4 level above 350cells/mm3. As compared those mothers who were not exposed to HAART mothers who were taking HAART during pregnancy had 8.2 fold increased risk of having low birth Weight.

On the other hand, baseline maternal CD4 level below 200/mm3[AOR(95%CI)= 5.37(1.89, 15.49)],having no PMTCT intervention during pregnancy [AOR (95%C.I) = 1.53(1.24, 3.05)],maternal BMI less than 18.5[AOR(95%C.I)=4.50(2.39, 9.27)], mother who started HAART before pregnancy [AOR(95%C.I)=1.82(1.02,3.81)] were associated with preterm delivery.

Mothers who had no PMTCT intervention had 1.63 times higher risk of having preterm birth as compared to those mothers who had PMTCT intervention. Moreover, mother who had started HAART before pregnancy had 1.82 fold increased risk of preterm delivery as compared those mothers who started on the pregnancy.

Table 4: Univariate analysis of factors associated with birth weight and gestational age at delivery among infant born to HIV positive mothers in Hospitals of North Gondar, Northwest Ethiopia from September1, 2009 to April 10, 2012.

Factors	LBW			PD		
	yes	no	P value	yes	no	P value
Age of mother			0.68			0.76
<19	1	6		1	6	
20-25	35	111		28	118	
26-30	36	153		28	161	
>31	17	57		12	62	
Residence			0.80			0.61
Urban	76	284		58	302	
Rural	12	41		10	43	
Educational status			0.33			0.53
Uneducated	40	141		33	148	
Primary school	27	76		21	82	
Secondary school	11	73		9	75	
Tertiary/College	8	20		3	25	
Higher degree	0	3		0	3	
Maternal occupation			0.24			0.23
Housewife	46	174		40	180	
Daily laborer	24	52		19	57	
Merchant	5	32		3	34	
Local drinking seller	1	10		0	11	
Gov't employee	7	24		3	28	
No occupation	5	29		3	31	
Marital status			0.19			0.97
Single	11	27		6	32	
Married	47	215		41	221	
Divorced	19	57		14	62	
Widowed	6	18		5	19	
Separated	6	8		3	11	
Pregnancy history			0.43			0.75
Primigravida	29	94		23	100	
Multigravida	59	221		44	236	

Obstetric complications			0.001			0.001
None	56	255		40	271	
APH	2	18		2	18	
Anemia	14	8		8	14	
Eclamsia	4	10		5	9	
PROM	12	27		13	26	
BMI			<0.0001			<0.0001
<18.499	43	34		34	43	
>18.5	40	230		27	243	
PMTCT intervention			0.015			0.002
No	10	76		24	62	
Yes	79	251		45	285	
HAART exposure			<0.0001			0.005
No	12	204		25	191	
Yes	77	123		44	156	
Time HAART initiated			<0.0001			0.001
Before pregnancy	44	28		22	50	
On pregnancy	33	95		22	106	
CD4 level (cell/mm3)			<0.0001			<0.0001
<200	39	45		38	46	
201-350	30	92		19	103	
>351	20	161		12	169	
WHO clinical stage			<0.0001			<0.0001
I	14	92		7	99	
II	17	122		10	129	
III	33	64		29	68	
IV	25	46		23	48	
Gestational age at birth			<0.0001			
>=37 weeks	34	313				
<37weeks	55	14				
Mode of labor			0.25			0.98
Induced	5	31		6	30	
Spontaneous	84	296		63	317	
Mode of delivery			0.62			0.86
Spontaneous vaginal	77	269		56	290	
Assisted/instrumental	8	37		8	37	
Operative	4	21		5	20	

NB: variables with P value less than 0.2 were entered into the multivariate analysis

Table 5: Bivariate and multivariate analysis of associated factors of low birth weight among infant born to HIV infected women in Public Hospitals of North Gondar zone, Northwest Ethiopia from September1, 2009 to April 10, 2012

Factors	**LBW**		**OR(95%C.I)**	
	Yes	**no**	**COR**	**AOR**
Maternal CD4 level(cells/mm3)				
<200	39	45	6.97[3.70,13.13]	4.24[1.85,9.69]*****
201-350	30	92	2.62[1.41,4.88]	1.13[0.53,2.37]
>351	20	161	1	1
Maternal WHO clinical stage				
Stage I	14	92	1	
Stage II	17	122	0.91[0.42,1.95]	
Stage III	33	64	3.38[1.68,6.83]*	
Stage IV	25	46	3.57[1.69,7.51]*	
Maternal BMI				
<18.499	43	34	7.27[4.14,12.74]	5.50[2.82,10.74]*****
>18.5	40	230	1	1
HAART exposure				
No	12	204	1	1
yes	77	123	10.64[5.56,20.34]	8.26[2.53,14.34]*****
Obstetric complications				
None	56	255	1	
APH	2	18	0.50[0.11,2.24]	
Anemia	14	8	7.96[3.19,19.90] *****	
Eclamsia	4	10	1.82[0.55,6.01]	
PROM	12	27	2.02[0.96,4.23]	
Gestational age				
>=37 weeks	34	313	1	1
<37 weeks	55	14	36.16[18.22,71,75]	28.14[12.69,62.34]*****

*****significant

Table 6: Bivariate and multivariate analysis of associated factors of preterm delivery among infant born to HIV infected women in North Gondar zone, Northwest Ethiopia from September1, 2009 to April 10, 2012

factors	PD		OR((95% C.I)	
	Yes	no	COR	AOR
Maternal CD4 level/cells/mm3				
<200	38	46	11.63[5.62,24.05]	5.37[1.86, 15.49]*
201-350	19	103	2.59 [1.21, 5.57]	0.83[0.28,2.41]*
>351	12	169	1	1
Maternal WHO clinical stage				
Stage I	7	99	1	
Stage II	10	129	1.09[0.40, 2.99]	
Stage III	29	68	6.03[2.49, 14.55]*	
Stage IV	23	48	6.77[2.71, 16.89]*	
Maternal BMI				
<18.499	34	43	7.11[3.90, 12.97]	4.52 [2.39, 9.27]*
>18.5	27	243	1	1
Time HAART initiated				
Before pregnancy	22	50	2.12[1.07, 4.18]	1.82[1.02,3.81]*
On pregnancy	22	106	1	1
Obstetric complications				
None	40	271	1	
APH	2	18	0.75[0.16,3.36]	
Anemia	8	14	3.87[1.52,9.81]*	
Eclamsia	5	9	3.76[1.20,11.79]*	
PROM	13	26	3.38[1.61,7.12]*	
PMTCT intervention				
No	24	62	2.45[1.39,4.32] *	1.53[1.24, 3.05]*
Yes	45	285	1	1
HAART exposure				
No	25	191	1	
Yes	44	156	2.15[1.26,3.67]*	

*significant

6. Discussion

While HIV/AIDS is not a major direct cause of neonatal death, maternal HIV status affects newborn survival by causing an increased risk of preterm, low birth weight and death in the neonatal period and infancy, even among those babies who do not become HIV-positive.(22) Preterm birth and low birth weight are the most common direct cause of newborn mortality. LBW contributes to 60% to 80% of all neonatal deaths (21).

The rate of low birth weight (21.4%) and preterm delivery (16.6%) in this study is higher than the global report (20) which is (15.5%) and the total prevalence rate in Ethiopia (15%) (18). The prematurity rate among HIV-infected pregnant women was twice than that in the general population according to study in France showed(63) and this study showed higher LBW and preterm delivery rate among HIV positive pregnant mothers than the general population. The current prevalence of low birth weight is almost comparable to study conducted in South Africa which is 22%(15),Ghana(22.5%) (64) and china(19.6%) (28) but higher than study from Tanzania(11.1%) (19),Thailand(12.6%) (65) and India (12.6%) (30) and higher rate of preterm delivery than in south Africa (13.3%) and china(9.8%).

The prevalence of pre-term delivery among HIV infected women in this study is higher than study from Thailand (37) which was 10.2% and lower than study from Ghana (64) which is (24.4%). The difference may be due either the treatment for the HIV, the study setting and time gap of study. prospective study conducted in Tanzania(19) found 23.5% incidence of preterm birth among HIV positive pregnant women which is higher than the present study and this difference could be the difference in the design of study.

Multivariate analysis have shown that lower baseline maternal CD4 count level, low maternal BMI,gestational age at birth below 37weeks and maternal exposure to HAART had statistically significant association with low birth weight.

Advanced maternal HIV disease is a recognized risk factor for preterm delivery as to the report of many studies (12, 55, 56) and studies from Kenya showed that HIV-infected women were 3 times more likely to deliver a low birth- weight baby, especially in the presence of HIV-related symptoms (25, 29) and the Univariate analysis in this study showed that advanced maternal WHO clinical stage especially In advanced WHO

clinical stage III (p=<0.0001) and stage IV(p=<0.0001) were associated with low birth weight and preterm birth, even though this variable didn't persist in the multivariate analysis .This can be explained that mother who are in advanced clinical stage could had severe cases of opportunistic infections which may affect the mother nutritional status and the in utero- fetal growth.

Early HAART initiation for all HIV-positive pregnant women (2, 8) and widespread use of HAART among HIV infected pregnant women has led to dramatic decreases in HIV transmission to the infant (9, 10) and decreases maternal morbidity(11-13).

However, this study has shown the significant association of maternal HAART exposure with LBW where those mothers who were on HAART had 8.2 fold increased risk of having LBW. This is consistent with previous studies demonstrating an association with preterm birth and in utero HAART exposure.(15) Similar studies suggested that the one who received HAART during pregnancy had 2.27 times higher risk in having LBW (40) and study conducted in Poland (39) which revealed that Pre-term deliveries were highly prevalent among women on HAART during pregnancy. It is also in line with the prospective study conducted in Côte d'Ivoire(53) where LBW was two-fold higher in the cohort that took three-drug HAART compared with the cohort that received short-course ARV prophylaxis. the one who received highly active antiretroviral therapy (HAART) had 2.27 times higher risk in having LBW as to the study in Thailand shown(37). Similarly a larger study in Botswana found that HAART-exposed infants were smaller for gestational age than unexposed infants (54). In contrary to this meta-analysis of 14 European and American clinical studies found no increase in risk of either PD or LBW with either any ARV drug receipt compared with no combination of ARV regimens (12) and the risk of LBW were not increased in any drug regimen groups(49).

The current study also report that lower maternal CD4 level is significantly associated with LBW; especially those with CD4 level below 200cells/mm3 had 4.24 higher risk of having lower birth weight than those mother with CD4 above 350cells/mm3. This may be explained as; the severely immuno-compromised mothers also may have many opportunistic infections and complications. Similar study have shown that women with a CD4 count <200 cells/mL were nearly twice as likely to have an adverse pregnancy outcome than those with a cell count of 500 cells/mL or more (16). Recent study in

china also indicated that Lower CD4 cell count; <100 cell/µl and CD4 cell count 100–199 cells/µl compared to CD4 ≥350 cells/µl and higher HIV RNA viral load [≥100 000 copies/ml at enrollment were the risk factors for LBW(28). However, one recent study depicted as there is no difference in LBW and PD among cohort of mothers with <200 CD4 cells and >500 CD4 cells respectively (60).

Poor maternal nutrition may be associated with adverse birth outcome in HIV positive women and one recent study(66) have revealed as maternal BMI below 21.8 had 1.82 higher risk of preterm delivery and 2.09 higher risk of LBW, and the current study multivariate analysis have shown 5.50 higher risk of LBW and 4.52 higher risk of preterm delivery. In relation to this the Univariate analysis showed that obstetric maternal complication especially maternal anemia during pregnancy had resulted in 3.87(p=0.004) and 7.96(p=<0.0001) higher risk of developing preterm delivery and LBW respectively. However the factor didn't persist in the multivariate analysis.

Preterm delivery was associated with low maternal CD4 level, having no PMTCT or untreated HIV infection among pregnant women, low BMI, mother who were already on HAART before pregnancy.

Those mothers who had no PMTCT/untreated pregnancy infection had 1.53 fold higher risk of preterm delivery as compared to the treated group. study conducted in Nigeria also have shown that pre-term birth were significantly higher among women with untreated-HIV infection in pregnancy compared with women who received HAART or prophylaxis from early pregnancy (52). This suggests the need for more strengthening of PMTCT intervention programme to decrease pregnancy complication.

Moreover, mother with CD4 level lower than 200 cells/mm3 had 5.37 higher risk of more preterm birth as compared to those with CD4 levels above 350cells/mm3 and this can be explained as; the risk severe immuno-suppression will lead the mother to have many infections and low weight gain. The finding is also consistent with many studies in Africa(15) and china.(28) However, one recent multi-centric study depicted as there is no difference in PD among cohort of mothers with <200 CD4 cells and >500 CD4 cells respectively(60).

This study also revealed that women who were already on HAART preconception had 1.82 fold increased risk of having preterm delivery compared to those who started later on pregnancy.

This finding is consistent with many studies in Europe and Africa. One study have shown that women who were using ARVs pre-conception had higher rates of PTD ((26.3% vs. 17.7%) respectively (38, 41). In line with this study conducted by European collaborative study observed a 2.1-fold increased risk when HAART was started before pre-conception (42, 43)and the risk of delivery before 34 weeks' gestation was 4.4-fold for those entering pregnancy on combination ARV regimens(42). This finding is also supported by study conducted in Poland (39) which revealed that Pre-term deliveries were highly prevalent among women on HAART during pregnancy, especially when therapy was started before or in the first trimester of pregnancy.

Limitation of the study

Due to the design of the study and as the study was conducted within routine clinical settings, this study were unfortunately not able to assess other known risk factors for LBW and PD which might also be associated with low birth weight and preterm birth like maternal smoking and alcohol intake history during pregnancy. In addition since the data are secondary there may be bias.

7. CONCLUSION AND RECOMMENDATION

Conclusion

The rate of low birth weight and preterm delivery among HIV positive pregnant mother who gave birth in public hospitals in North Gondar zone is very high. The finding of this study for the associated factors of low birth weight suggest that low maternal baseline CD4 count level, low maternal BMI,preterm delivery, maternal HAART exposure were risk factors for low birth weight.

On the other hand low baseline maternal CD4 count level, having no PMTCT intervention/untreated HIV infection, low maternal BMI, and mother who were on HAART before pregnancy were associated with preterm delivery. This suggests the need for early intervention to increase the maternal CD4 level and reduce the infections before conception in those mothers with intention to have child. The findings are consistent with many African and European based study.

RECOMENDATION

To health institutions /Hospitals, health centers;

- The earlier identification and treatment of mothers before their conception to delay conception until CD4 cell count increased and HIV viral load decrease, especially in those in advanced clinical stage.
- Encouraging and educating severely immuno-compromised HIV-infected women who plan to become pregnant to wait until immune restoration may help to reduce the risk of LBW and PD.
- Family planning programme should be strengthened more, giving special attention to HIV infected mothers especially who are on HAART and in advanced clinical stage to delay pregnancy
- Strengthening education and nutritional supplementation for HIV infected mothers.
- Strengthening PMTCT services not to miss treatment for all HIV infected women having intention to have children.

For HIV positive mothers;

- It is better if the mothers report early to their doctors when they have intention to give birth so as to get appropriate advice and intervention before conception.

For researchers:

- It would be very important if further prospective kind of study is done in future to further deal on the problem by including the other important variables.

REFERENCE

1.UNAIDS WHO. AIDS epidemic update.World Health Organization 2009.

2.UNAIDS/WHO. Report on the Global AIDS Epidemic. Geneva: World Health Organization.2008.

3.ANTIRETROVIRAL DRUGS FOR TREATING PREGNANT WOMEN AND PREVENTING HIV INFECTION IN INFANTS ; Recommendations for a public health approachWorld Health Organization, 2010.

4.Towards universal access: Scaling up priority HIV/AIDS interventions in the health sector. Progress Report Available: http://www.who.int/hiv/pub/2010progressreport/report/en/index.html. [database on the Internet]. [cited Accessed February 21, 2011.].

5.WorldHealthOrganization. Towards Universal Access Progress 2010 [Retrieved on January 8, 2011]; Available from: http://www.who.int/hiv/pub/2009progressreport/en/.

6.Federal HIV/AIDS Prevention and Control Office:Prevention of Mother to Child Transmission 2010 [http://www.etharc.org/], Retrieved on January 6, 2011.

7.Tilahun Nigatu YW. Analysis of the Prevention of Mother-to-Child Transmission (PMTCT) Service utilization in Ethiopia: 2006-2010;2011,8:6Reproductive Health doawnloaded at; http://wwwreproductive-health-journalcom/content/8/1/6.

8.Hargrove JW HJ, Grp ZS. Mortality among HIV-positive postpartum women with high CD4 cell counts in Zimbabwe. AIDS. 2010;24(3):F11-F4.

9.Kourtis AP. Antiretroviral Drug Use during Pregnancy and Risk of Premature Delivery: Is There a Connection? The Journal of Infectious Diseases 2010;201:978-80.

10.Patrice Tchendjou CS-E, Annie Nga, Mathurin Tejiokem, Anfumbom Kfutwah, Anne Njom Nlend, Landry Tsague, Anne Ce´ cile Bissek, Daniel Ekoa, Joanna Orne-Gliemann, Dominique Rousset, Re´ gis Pouillot, Franc¸ois Dabis. Effectiveness of Multidrug Antiretroviral Regimens to Prevent Mother-to-Child Transmission of HIV-1 in Routine Public Health Services in Cameroon PLoS ONE. 2010;5(4).

11.Hoosen Coovadia. Antiretroviral Agents - How Best to Protect Infants from HIV and Save Their Mothers from AIDS N Engl J Med. July 15,2004;351:289-92.

12.Kourtis AP SC, Jamieson DJ, Lau J. Use of antiretroviral therapy in pregnant HIV-infected women and the risk of premature delivery: a meta-analysis. AIDS. 2007 Mar 12;21(5):607-15.

13.Nigel C. Rollins HMC, et al. Pregnancy Outcomes in HIV-Infected and Uninfected Women in Rural and Urban South Africa. J Acquir Immune Defic Syndr. 2007;44:321-8.

14.Denise Naniche AB, María Lahuerta , Anna Berenguera , Inacio Mandomando , Sergi Sanz , John J. Aponte , Betuel Sigauque , Pedro L. Alonso , and Clara Menéndez. Impact of Maternal Human Immunodeficiency Virus Infection on Birth Outcomes and Infant Survival in Rural Mozambique. Am J Trop Med Hyg 2009;80(5):870-6.

15.Karin van der Merwe RH, Vivian Black, Matthew Chersich, Ashraf Coovadia and Helen Rees Birth outcomes in South African women receiving highly active antiretroviral therapy: a retrospective observational study: . Journal of the International AIDS Society 2011;14(42).

16.Rollins NC CH, Bland RM, Coutsoudis A, Bennish ML, Patel D, Newell ML,. Pregnancy outcomes in HIVinfected and uninfected women in rural and urban South Africa. J Acquir Immune Defic Syndr. 2007;44:321-8.

17.Langston C LD, Hammill HA, Popek EJ, Kozinetz CA, Kline MW, Hanson IC, Shearer WT, . Excess intrauterine fetal demise associated with maternal human immunodeficiency virus infection. J Infect Dis. 1995;172:1451-60.

18.UnitedNationsChildren'sFundandWorldHealthOrganization. Low Birthweight: Country,regional and global estimates. UNICEF, New York2004.

19.Dreyfuss ML, Msamanga GI, Spiegelman D, Hunter DJ, Urassa EJ, Hertzmark E, et al. Determinants of low birth weight among HIV-infected pregnant women in Tanzania. American Journal of Clinical Nutrition. 2001;74:814-26.

20.SIZA JE. Risk factors associated with low birth weight of neonates among pregnant women attending a referral hospital in northern Tanzania. Tanzania Journal of Health Research 2008;10(1).

21.WorldHealthOrganization. Care of the preterm and/or low-birth-weight newborn. accessed on March 08,2012.

Available from: http://www.who.int/maternal_child_adolescent/topics/newborn/care_of_preterm/en/.

22.Temmerman M PF, Mirza NB, Ndinya-Achola JO, Wamola IA,, al. NNe. Infection with HIV as a risk factor for adverse obstetrical outcome. Opportunities for African Newborn. AIDS 1990;4(11):1087-93.

23.Bulterys M CA, Munyemana S, Kurawige JB, Nawrocki P, Habimana P et al. . Maternal human immunodeficiency virus 1 infection and intrauterine growth: a prospective cohort study in Butare, Rwanda. Pediatr Infect Dis J. 1994;13(2):94-100.

24.Brocklehurst P FR. The association between maternal HIV infection and perinatal outcome: a systematic review of the literature and meta-analysis. Br J Obstet Gynaecol. 1998 Aug;105(8):836-48.

25.Katia Kastetbon Jl, ValerianeLorey,et al. Low birth weight in Infant born to African HIV-infected Women:Relationship with maternal body weight during pregnancy. Journal of Tropical Pediatrics. June 1999;45.

26.A.O.Olatunji, A.O.Sunji-Oda, A.T.Oladapo. Intrapartum HIV screening at a University Hospital in Nigeria. Nigerian Medical practicioner. November 6,2008;53(6).

27.Marta Lopeza FF, Sandra Hernandeza, Montserrat Loncab, Raul Garciaa, Montse Palacioa and Oriol Colla Association of HIV Infection With Spontaneous and Iatrogenic Preterm Delivery. AIDS. 2012;26(1):37-43.

28.Lan Y, Wen-ying L, Chen RY, Zhi-rong T, PANG Jun GX-z, Xiu-ning M, et al. Pregnancy outcomes and risk factors for low birth weight and preterm delivery among HIV-infected pregnant women in Guangxi, China. Chinese Medical Journal 2012;125(3):403-9.

29.Braddick MR KJ, Embree JB, et al. Impact of maternal HIV infection on obstetrical and early neonatal outcome. . AIDS. 1990;4:1001-5.

30.Patil S BR, Sambarey P, Gupte N, Suryavanshi N, Sastry J, Bollinger RC, Gupta A, Shankar A. Impact of maternal human immunodeficiency virus infection on pregnancy and birth outcomes in Pune, India. AIDS Care. 2011 Dec;23(12):1562-9.

31.Tuomala RE WD, Li D, Vajaranant M, Pitt J, Hammill H, et al. . Improved obstetrical outcomes and few maternal toxicities are associated with antiretroviral therapy including highly active antiretroviral therapy during pregnancy. . J Acquir Immune Defic Synd. 2005:38:449-73.

32.World Health Organization.Antiretroviral therapy for HIV infection in adults and adolescents: recommendations for a public health approach; 2006. http://www.who.int/hiv/pub/guidelines/artadultguidelines.pdf (Accessed 8 november 2010).

33.Jan Walter Mww, N ancyS cott,P risca Kasonde,M oses Sinkala,sC hipepoK ankasa,S h uaibK auchali,GraceM . AldrovandiD,o naldM . Thea,a nd LouiseK uhn. Reduction in Preterm Delivery and Neonatal Mortality after the Introduction of Antenatal Cotrimoxazole Prophylaxis among HIV-Infected Women with Low CD4 Cell Counts The Journal ofInfectious Diseases. 2006;194:151.

34.Walter J MM, Scott N, Kasonde P, Sinkala M, Kankasa C, Kauchali S, Aldrovandi GM, Thea DM, Kuhn L. Reduction in preterm delivery and neonatal mortality after the introduction of antenatal cotrimoxazole prophylaxis among HIV-infected women with low CD4 cell counts. Journal of Infectious Disease. 2006 Dec 1;194(11):1510-8.

35.Walter J MM, Scott N et al. Cotrimoxazole prophylaxis and adverse birth outcomes among HIV-infected women in Lusaka, Zambia;Denver, Colorado. 13th Conference on Retroviruses and Opportunistic Infections,5-8 February 2006.

36.Hoffman RM BV, Technau K, van der Merwe KJ, Currier J, Coovadia A, Chersich M. . Effects of Highly Active Antiretroviral Therapy Duration and Regimen on Risk for Mother-to-Child Transmission of HIV in Johannesburg, South Africa. Journal of Acquired Immune Deficiency Syndromes Jaids. 2010;54(1):35-41.

37.Darin Areechokchai CB, Benjaluck Phonrat,Punnee Pitisuttithum, and Wirach Maek-a-Nantawat,. Pregnancy Outcomes Among HIV-Infected Women Undergoing Antiretroviral Therapy The Open AIDS Journal, 2009;3: 8-13.

38.E S Machado CBH, T T Costa, S A Nogueira, R H Oliveira, T F Abreu, L A Evangelista, I F A Farias, R T C Mercadante, M F L Garcia, R C Neves, V M Costa, J S Lambert. Pregnancy outcome in women infected with HIV-1 receiving combination antiretroviral therapy before versus after conception. Sexualy Transmitted Infection 2009;85:82-7.

39.Kowalska A NT, El Midaoui A, Burkacka E. Effect of antiretroviral therapy on pregnancy outcome in HIV-1 positive women. Med Wieku Rozwoj 2003 Oct-Dec;7(4 Pt 1):459-68.

40.Asavapiriyanont S KS. Prevalence of low birthweight infants in HIV-infected women delivered in Rajavithi Hospital. Journal of Medical Association Thailand March 2011 94 (2):66-70.

41.European Collaborative Study SMaCCS. Combination antiretroviral therapy and duration of pregnancy.AIDS. 2000;14:2913-20.

42.Thorne C PD, Newell ML, for the European Collaborative study. . Increased risk of adverse pregnancy outcomes in HIV-infected women treated with highly active antiretroviral therapy in Europe. AIDS 2004;18:2337-9.

43.Machado ES HC, Costa TT, et al. Pregnancy outcome in women infected with HIV-1 receiving combination antiretroviral therapy before versus after conception. Sex Transm Infect. 2009 Apr;85(2):82-7.

44.Schulte J DK, Sukalac T, Bohannon B, Fowler MG. Declines in low birth weight and preterm birth among infants who were born to HIV-infected women during an era of increased use of maternal antiretroviral drugs:. Pediatric Spectrum of HIV disease1989-2004. Pediatrics 2007;119:e900-e6.

45.Tuomala RE SD, Mofenson LM, et al. Antiretroviral therapy during pregnancy and the risk of an adverse outcome. N Engl J Med. 2002 Jun 13;346(24):1863-70.

46.Tuomala RE WD, Li D, et al. Improved obstetric outcomes and few maternal toxicities are associated with antiretroviral therapy, including highly active antiretroviral therapy during pregnancy. J Acquir Immune Defic Syndr. 2005 Apr 1;38(4):449-73.

47.Ruth E. Tuomala DES, Lynne M. Mofenson et al. ANTIRETROVIRAL THERAPY DURING PREGNANCY AND THE RISK OF AN ADVERSE OUTCOME. New England Journal of Medicine, June 13, 2002;346(24).

48.Szyld EG WE, Freimanis L, et al. , Maternal antiretroviral drugs during pregnancy and infant low birth weight and pretermbirth. AIDS 2006;20:2345-53.

49.Cotter AM GA, Duthely ML, Luke B, O'Sullivan MJ. . Is antiretroviral therapy during pregnancy associated with an increased risk of preterm delivery, low birth weight, or stillbirth? J Infect Dis. 2006 May 1;193(9):1195-201.

50.Steketee RW NB, Parise ME, Menendez C, The burden of malaria in pregnancy in malaria-endemic areas. . Am J Trop Med Hyg. 2001; 64:28-35.

51.Barbara J. Turner CJN, James Cocroft, Thomas R. Fanning, Sue Marcus, and Walter W. Hauck,. Improved Birth Outcomes Among HIV-Infected Women With Enhanced Medicaid Prenatal Care. American Journal of Public Health. January 2000;90(1).

52.Joseph O BO, Michael E. Pregnancy outcome among HIV positive women receiving antenatal HAART versus untreated maternal HIV infection Journal of Coll Physicians Surg Pak. 2011 Jun;21(6):356-9.

53.Ekouevi DK CP, Becquet R, Tonwe-Gold B, Horo A, Thiebaut R, Leroy V, Blanche S, Dabis F, Abrams EJ. Antiretroviral therapy in pregnant women with advanced HIV disease and pregnancy outcomes in Abidjan, Cote d'Ivoire. Aids 2008;22:1815-20.

54.Chen J. Risk Factors for Adbverse Pregnancy Outcomes among HIVinfected Women in Gaborone, Botswana. 16th Conference on Retroviruses and Opportunistic Infections;Montreal,Canada,2009.

55.Stratton P TR, Abboud R, et al. . Obstetric and newborn outcomes in a cohort and HIV-infected pregnant women: a report of the Women and Infants Transmission Study. J Acquir Immune Defic Syndr Hum Retrovirol. 1999;20:179-86.

56.Powis KM, Kitch D, Ogwu A, Hughes MD, Lockman S, Leidner J, et al. Increased Risk of Preterm Delivery Among HIVInfected Women Randomized to Protease Versus Nucleoside Reverse Transcriptase Inhibitor-Based HAART During Pregnancy. Journal of Infectious Diseases 2011;204:506-14.

57.Grosch-Woerner I PK, Maier RF,et al.Increased rate of prematurity associated with antenatal antiretroviral therapy in a German/Austrian cohort of HIV-1-infected women. HIV Med 2008,Jan; 9(1):6-13.

58.Patel K SD, Brogly SB, Livingston EG, Stek AM, Bardeguez AD, Tuomala RE, Int Maternal Pediat Adolescent AID. . Prenatal Protease Inhibitor Use and Risk of Preterm Birth among HIV-Infected Women Initiating Antiretroviral Drugs during Pregnancy. Journal of Infectious Diseases. 2010;201(7):1035-44.

59.Michele L Dreyfuss GIM, Donna Spiegelman, David J Hunter, Ernest JN Urassa, Ellen Hertzmark, Wafaie W Fawzi. Determinants of low birth weight among HIV-infected pregnant women in Tanzania. American Journal of Clinical Nutrition 2001;74:814-26.

60.Group TKBS. Eighteen-Month Follow-Up of HIV-1–Infected Mothers and Their Children Enrolled in the Kesho Bora Study Observational Cohorts Journal of Acquired Immune Deficiency Syndrome. 2010;54:533-41.

61.CSA Office Gondar branch,Ethiopia 2000 Report.

62.North Gondar Zonal Health office,Ethiopia, Annual plan and Achievement Report, July 2008.

63.Sibiude J, Warszawski J, Tubiana R, Dollfus C, Faye A, Rouzioux C, et al. Premature Delivery in HIV-Infected Women Starting Protease Inhibitor Therapy During Pregnancy: Role of the Ritonavir Boost? Clinical Infectious Disease. 2012 Mar 28.

64.LaarA.K., AmpofoW., TuakliJ.M., NorgbeG.K., QuakyiI.A. Preterm delivery and low birth weight among neonates born to HIV-positive and HIV-negative Ghanaian women. Journal of Public Health and Epidemiology December 2010;2(9):224-37.

65.Asavapiriyanont S, Kasiwat S. Prevalence of low birthweight infants in HIV-infected women delivered in Rajavithi Hospital. Journal of Medical Association ThailandMarch 2011 94 (2):66-70.

66.Mehta S, Manji KP, Young AM, Brown ER, Chasela C, Taha TE, et al. Nutritional indicators of adverse pregnancy outcomes and mother-to-child transmission of HIV among HIV-infected women. American Journal of Clinical Nutrition. 2008;87:1639-49.

9. ANNEXES

9. 1 Data extraction format

no	VARIABLES	Delivery Chart no :---------- ANC/PMTCT card no ----- ART clinic chart no ……..
	Site of data collection	*Gondar hospital* *Debark hospital* *Metemma Hospital*
	A. CURRENT BIRTH OUTCOME HISTORY	
1	Infant date of birth	
2	Infant place of birth	
3	Sex of newborn	Male Female
4	Birth weight	
5	Gestational age at delivery	<34 weeks 34-37weeks >37weeks
6	Apgar score at 5 minute	
	Admission to Neonatal care unit for newborn complications	1. Yes 2. no
8	maternal weight	1. Baseline:_____ 2. 2nd visit:_____ 3. 3rd Visit:_____
9	maternal height	
10	BMI	
12	Condition of newborn/fetal outcome	1. alive 2. still birth 3. early death 4. birth defect:_____
14	Mode of labor	1. induced b/c of complication 2. normal labor
15	Mode of delivery	1. Normal vaginal 2. Instrumental 3. C/s before labor 4. C/s after labor/PROM 5. others
	B. MOTHER SOCIODEMOGRAPHIC HISTORY	

18	Age of mother at delivery		
19	residence	1. Urban 2. rural	
20	Educational level	1. Uneducated 2. Primary 3. Secondary 4. college	
21	occupation	1. Gov't employee 2. Merchant 3. Daily laborers 4. Housewife 5. other	
22	Marital status	1. Single 2. Married 3. Divorced 4. Widowed 5. separated	
23	religion	1. Orthodox 2. Muslim 3. Protestant 4. others	
24	parity	1. Primigravida 2. multigravida	
16	gravidity	1. Primigravida 2. multigravida	
C. OBSTETRIC HISTORY			
20	Obstetric complications?	1. APH 2. PROM 3. Anemia 4. others	
21	ANC follow-up?	1. Yes 2. No	
22	Duration of ANC?	1. Once 2. Twice 3. Three times 4. >three	
D. ARVS TREATMENT AND FOLLOW UP HISTORY			
26	When mothers HIV infection known?	1. Before pregnancy 2. On pregnancy 3. On delivery (unbooked)	
28	Duration on Cotrimoxazole during pregnancy?	1. Not at all/no cotrimoxazole 2. <10weeks 3. 10-16weeks 4. 16-32weeks 5. >32weeks 6. The whole duration of pregnancy	

29	What type of ARVs treatment the mother was given during pregnancy?	1. HAART 2. Short course regimen prophylaxis 3. other	
27	When is this ARVs prophylaxis started?	1. Before current pregnancy 2. After pregnancy	
28	If ARV prophylaxis started on pregnancy; when?	1. >=37weeks 2. 28-36weeks 3. 15-27weeks 4. <=14weeks	
29	What type of short course regimen/prophylaxis given?	1. AZT monotherapy 2. sdNVP 3. sdNVP+ AZT 4. sdNVP+ AZT+3TC 5. only Cotrmoxazole	
30	When is the HAART started?	1. Before current pregnancy 2. After pregnancy	
31	• If HAART started before current pregnancy: when is her pregnancy reported to ANC clinic or Doctor?	1. >=37weeks 2. >28-36weeks 3. 15-27weeks 4. <=14weeks	
33	If HAART started on pregnancy when (at what gestational age) it started?	1. >=37weeks 2. >28-36weeks 3. 15-27weeks 4. <=14weeks	
34	Median duration on HAART before delivery?	1. <5 weeks 2. 5-6weeks 3. 7-8 weeks 4. >8weeks	
35	HAART regimen type?		
38	Baseline CD4 level of pregnant mother?	1. <200 ml/d 2. 200-350 ml/d 3. 350-500 ml/d 4. >500 ml/d	
41	Baseline WHO stage on pregnancy?	1. Stage I Stage II 2. Stage III Stage IV	
42	Treatment complications on pregnancy**:**	1. No complications 2. Anemia 3. Toxicities 4. treatment failure	
43	COMORBIDITIES	1. DM 2. HTN 3.TB on pregnancy 2. STI 5.Treatment for malaria	
44	Treated for TB on Pregnancy?	1. Yes 2.No	
45	Treated for STI on pregnancy?	1. Yes No	

9.2. Fig 1: Conceptual framework showing predicting factors of birth Outcome among HIV infected Women